Fostering the Development of Infants & Toddlers Born Prematurely: Part I—Understanding Medical Complications Associated with Prematurity and the Potential Impact on Development

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Presentation Objectives
- ...become aware of preemie statistics for the United States and South Carolina as well as the outcomes associated with prematurity.
- ...develop an understanding of neonatal diagnosis associated with prematurity.
- ...become familiar with the potential developmental impact of such diagnosis.

Definitions
- Preterm infant: Born < 37 weeks gestation
- Moderately preterm: 32-36 weeks gestation
- Very preterm: <32 weeks gestation
- LBW infant: Born <2,500 grams
- VLBW infant: Born <1,500 grams
- ELBW infant: Born <1,000 grams

Preemie Statistics
...Rationale for Monitoring the Development of Infants Born Prematurely

Preterm, US 2004
www.marchofdimes.com/peristats/
- 1 in 8 babies born prematurely
- 12.5%
- N=508,358

Very Preterm, US 2004
www.marchofdimes.com/peristats/
- 2% born very preterm
- N=81,645
1.5% VLBW
N=60,640

8,752 preterm births
1 in 6 babies (15.5%) born prematurely
Between 1994 and 2004, rate of infants born prematurely increased 25%

1,598 babies (28%) born very prematurely
Healthy People 2010 goal ≤1.1%

1 in 10 (10.2%) LBW (1500-2499g)
Black infants (15%) were 2x more likely than Hispanic infants (6.5%)
Multiples 8x more likely than singleton

1,186 (2.1%) VLBW (<1500g)
Healthy People 2010 goal ≤0.9%

Although many factors go into predictions regarding morbidity, infants born earliest and at the smallest weights have the highest risk of developing disabilities.
The rate of overall disability in infants born extremely premature is 49% and the rate of severe disability is 23% (Wood, NS, et al., 2000).
Morbidity at 18-22 Months of Survivors Born at 22-26 Weeks Gestation in 1997-1998
NICHD Neonatal Network
(Vohr et al., Pediatrics, 2005)

- Minimal or No Disability: 55%
- Moderate or Severe Disability: 45%

Risk of Death or Disability at 6 Years: Infants Admitted at 22-25 Weeks Gestation in 1995
EPICure Study
(Marlow et al., NEJM, 2005)

- Death Before Discharge: 58%
- Lost to Follow-up: 11%
- Death After Discharge: 1%
- Severe Disability: 7%
- Other Disability: 17%
- No Disability: 6%

Risk of Death or Disability at 6 Years: Infants Admitted at 22-25 Weeks Gestation in 1995
EPICure Study
(Marlow et al., NEJM, 2005)

- No Disability: 20%
- Other Disability: 57%
- Severe Disability: 23%

IVH
Intraventricular Hemorrhage

- Bleeding into the ventricular system of the premature brain.
- Four grades:
  1. Germinal Matrix Bleed
  2. Ventricular Bleed
  3. Ventricular Bleed + dilation of ventricle
  4. Parenchymal bleed

Normal Head Ultrasound
Grade II - IVH
Bleed without significant ventricular dilation.

Grade III - IVH
Bleed plus ventricular dilation.

- Bleed into surrounding parenchymal tissue.
  - White echodensities

Mortality
- Grade I: 5%*
- Grade II: 10%*
- Grade III: 20%
- Grade IV: 50%
*Not increased, when controlled for prematurity.

Neurologic Sequelae
- Grade I/II IVH
  - No increased risk for major disability.
- Grade III IVH
  - ~30% with major disability at school age most common are spastic diplegia and quadriplegia.
  - Cognitive and neuromotor disability common, ~50% require special education.
- Grade IV IVH
  - Little data b/c ↓ frequency ↑ mortality.
  - 80% manifest symptoms of major disability during infancy.
  - Most common: contralateral hemiparesis; cognitive and neuromotor ability affected.

PHH
Post Hemorrhagic Hydrocephalus
Special Consideration: PHH

- Most common with Grade III/IV IVH:
  - Grade III ~20%
  - Grade IV >60%
- Inflammation, clot, protein and debris results in ventricular obstruction and then progressive and rapid accumulation of CSF.
- Severe ventricular dilation increases intracranial pressure and destroys surrounding parenchyma.
- TX with serial spinal taps or VP shunt.

PVL
Periventricular Leukomalacia

- Result of Hypoxic Ischemic Encephalopathy (HIE):
  - Clinical manifestation of neonatal asphyxia.
  - Criteria for Diagnosis:
    - Profound metabolic or mixed acidosis.
    - Apgar 0-3 for > 5 mins.
    - Neonatal neurologic manifestations include seizures, coma and hypotonia.
    - Multi system organ dysfunction (CV, GI, renal).
- Involves necrosis of periventricular white matter of the brain.
- Commonly results in CP; possibly MR & visual impairments.

BPD
Bronchopulmonary Dysplasia

- Need for oxygen on DOL #28.

BPD

Normal lung x-ray
X-ray depicting BPD
NEC
Necrotizing Enterocolitis

Definition
Necrotizing Enterocolitis
- Death of tissue
- Small intestine inflammation

Inflamed Bowel
- Inflamed bowel
- Cross section of inflamed bowel

Bowel Gas Pattern
- Normal
- Dilated loops of bowel

Prognosis
- Bowel Surgery:
  - Resection
  - Long-term parenteral nutrition
  - Enterostomy care, short gut syndrome, failure to thrive
  - NEC with perforation: 20-40% mortality
- Uncomplicated Course:
  - Growth, nutrition, GI function appear to catch up by the end of the first year

ROP: Retinopathy of Prematurity
- ROP is a progressive eye disease.
- It begins with some mild changes in the vessels, and may progress on to more severe changes.
- The zone of ROP describes the location.
- The stage of ROP describes how far along in this progression the vessels have reached. Concerns ≥Stage 4 ROP.
ROP Zone

ROP

- Stage 4
  - Refers to a partial retinal detachment.
  - Further categorized depending upon the location of the retinal detachment.
    - Stage 4A, detachment does not include the macula—vision may be good.
    - Stage 4B, macula is detached—visual potential is markedly decreased.
- Stage 5
  - Implies a complete retinal detachment.
  - Eyes with stage 5 ROP usually have no useful vision, even if surgery is performed to repair the detachment.

ROP Screening

- 1st exam: 4-6 weeks of life for:
  - Preemies born <1500g or <28wks
  - Any severely ill preemie
  - Any preemie with prolonged oxygen therapy
- Then, exams every 2 weeks or more often until discharge
- Follow-up post discharge:
  - Regressed ROP without scars: until full vascularization then annually
  - Regressed ROP with scars: annually
  - Progressed ROP (detachment): ongoing care

ROP: Treatment

- Based on results of the ETROP study, treatment is recommended for any eye with:
  - Zone I any stage with plus disease,
  - Zone I, stage 3 without plus disease, or
  - Zone II stage 2 or 3 with plus disease.
- Cryotherapy: Freezing of avascular retina anterior to the retina. Peak age is time of discharge.
- Laser therapy: Uses laser beam. Better tolerated, easier, faster, requires less sedation & better reaches most important area for vision (posterior retina).
- Scleral Buckle & Vitrectomy Procedures: Heroic. Some anatomic success but less functional improvement.

ROP: Common Sequelae

- Regressed without scars: strabismus, amblyopia, myopia.
- Regressed with scars: thinning of retina, retraction, retinal tears-retinal dragging-detachment-glucoma, vision loss.
- Progressed ROP: reduced visual acuity, visual field loss, reduction in contrast sensitivity, nystagmus, glaucoma.

As & Bs

- Apnea: pause in breathing >20 seconds.
- Bradycardia: fall in heart rate, often accompanies breathing lapse.
- Incidence: 10% preemies, >40% VLBW.
- Treatment: theophylline or caffeine used to stimulate breathing, rocker beds.
- Persistent apnea correlated with bad prognosis:
  - May indicate brain damage.
  - May be precursor to SIDS:
    - 20% of all SIDS are preemies.
    - Occurs during first 5 months of life.
  - Babies w/ As at discharge go home on monitor.
PDA: Patent Ductus Arteriosus

- Incidence: 21% 500-1700 grams, 50% 500-1000 grams, > if received surfactant.
- Cause: In preemies w/ RDS the O2 level in the blood isn’t high enough to stimulate contraction of the ductus.
- Treatment
  - Medication (indomethacin) to stimulate contraction of the muscular walls of the ductus arteriosus, closing it in most cases.
  - Surgical ligation to close the ductus.

SGA

- Newborn with weight < 10th %ile for GA.
- Problems:
  - Remain short and underweight throughout life.
  - Incidence of developmental disabilities higher compared to babies AGA.
  - PT SGA: MR, CP.
- Medical Care: deliver in NICU, outcome better than transports.

RSV

Respiratory Syncytial (sin-sish-shul) Virus

www.synagis.com

RSV…More Facts

- RSV disease is universal and occurs in nearly all children by 2 years of age.
- RSV is the leading cause of hospitalization in infants <1 year old.
- RSV epidemics are local and local virology is the best way to determine timing of RSV prophylaxis.
- Effective therapeutic options are not available.
- Synagis® (palivizumab) is the only immunoprophylaxis option approved by the FDA.
- Synagis is generally well tolerated and effective in preventing hospitalizations due to severe RSV infections.

RSV: Signs & Symptoms

- Mild: moderate tachypnea, rhinorrhea, low-grade fever, and, frequently, otitis media. Recovery occurs after an illness of 7 to 12 days.
- Severe: coughing and wheezing followed by dyspnea; severe tachypnea is common; in cases of extreme hypoxemia, respiratory failure occurs.
- In high-risk infants, respiratory failure severe enough to require airway intubation can occur early in the course of illness.

RSV Transmission

- Transmitted by droplets, large particles, and fomites.
- RSV survives up to 6 hours on stethoscopes and up to 12 hours on hard, nonporous surfaces.
- Over 50% of medical personnel infected when RSV is prevalent in community.
- Hospital acquired infection remains a serious problem.
2006 AAP Guidelines for RSV Prophylaxis

≤ 28 wk GA: Consider Synagis® (palivizumab) if ≤ 12 mo of age at start of RSV season

29–32 wk GA: Consider Synagis if ≤ 6 mo of age at start of RSV season

32–35 wk GA: Consider Synagis if < 6 mo of age at start of RSV season with ≥ 2 risk factors

Percent Positive Antigen Detection for RSV

![Graph showing percent positive antigen detection for RSV with different regions indicated by line colors: South, Midwest, Northeast, West, Florida.]

Diagnosis to Early Intervention...UMMS Study

- UMMS NICU Follow-Up Program & Baltimore City Infants & Toddlers Program (BITP) conducted a collaborative retrospective study to:
  - explore the trends in follow-up of infants born prematurely.
  - understand the patterns of early intervention & special preschool services needed by children born prematurely.


Methods

- Retrospective reviews UMMS NICU Follow-up Clinic’s database and the BITP database were conducted.
  - Baltimore City residents.
  - Gestational age < 37 weeks.
  - Referred to UMMS’ NICU Follow-up Clinic.
  - 399 infants identified for study, 286 attended at least one visit, 154 followed until age 3 years.

High Probability Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Attend (N=286)</th>
<th>Never Attend (N=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall, 64.3% automatically eligible</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Birthweight (BW) ≤ 1200g</td>
<td>36.9% (100)</td>
<td>46% (52)</td>
</tr>
<tr>
<td>Cytomegalovirus (CMV)</td>
<td>1.5% (4)</td>
<td>0</td>
</tr>
<tr>
<td>Congenital Anomalies</td>
<td>4.1% (11)</td>
<td>0</td>
</tr>
<tr>
<td>Congenital Infections</td>
<td>1.9% (5)</td>
<td>1.7% (1)</td>
</tr>
<tr>
<td>Genetic Anomalies</td>
<td>0.4% (1)</td>
<td>0</td>
</tr>
<tr>
<td>Hypoxic-Ischemic Encephalopathy (HIE)</td>
<td>0.7% (2)</td>
<td>1.4% (1)</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>3.4% (9)</td>
<td>6.6% (4)</td>
</tr>
<tr>
<td>Intraventricular Hemorrhage (IVH) III/IV</td>
<td>2.2% (6)</td>
<td>1.7% (1)</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>0.4% (1)</td>
<td>0</td>
</tr>
<tr>
<td>Other Brain Abnormality (e.g., PVL)</td>
<td>4.1% (11)</td>
<td>5% (3)</td>
</tr>
<tr>
<td>Seizures</td>
<td>0.7% (2)</td>
<td>1.7% (1)</td>
</tr>
<tr>
<td>Sensory Impairment</td>
<td>0.4% (1)</td>
<td>3.4% (2)</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>0.4% (1)</td>
<td>1.7% (1)</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>3.7% (10)</td>
<td>8.3% (5)</td>
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</tbody>
</table>

Other Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Attend (N=286)</th>
<th>Never Attend (N=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchopulmonary Dysplasia (BPD)</td>
<td>39.7% (106)</td>
<td>20% (12)</td>
</tr>
<tr>
<td>Gastroesophageal Reflux (GER)</td>
<td>9.7% (26)</td>
<td>6.7% (4)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>12.4% (35)</td>
<td>8.3% (5)</td>
</tr>
<tr>
<td>Intrauterine Growth Retardation (IUGR)</td>
<td>2.6% (7)</td>
<td>3.3% (2)</td>
</tr>
<tr>
<td>Meconium Aspiration</td>
<td>7% (1)</td>
<td>0</td>
</tr>
<tr>
<td>Meningitis</td>
<td>2.6% (7)</td>
<td>3.3% (2)</td>
</tr>
<tr>
<td>Necrotizing Enterocolitis (NEC)</td>
<td>10.5% (28)</td>
<td>6.7% (4)</td>
</tr>
<tr>
<td>Patent Ductus Arteriosus (PDA)</td>
<td>22.2% (70)</td>
<td>15% (9)</td>
</tr>
<tr>
<td>Respiratory Distress Syndrome (RDS)</td>
<td>71.2% (190)</td>
<td>53.3% (32)</td>
</tr>
<tr>
<td>Retinopathy of Prematurity (ROP)</td>
<td>27.3% (73)</td>
<td>23.3% (14)</td>
</tr>
<tr>
<td>Small for Gestational Age (SGA)</td>
<td>4.1% (11)</td>
<td>13.3% (8)</td>
</tr>
<tr>
<td>Tone Abnormal</td>
<td>1.5% (4)</td>
<td>3.4% (2)</td>
</tr>
</tbody>
</table>
Trends in Disciplines Seen

Age When Direct Early Intervention Service Initiated

Diagnoses Correlated with Obtaining Specific Services

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>PT</th>
<th>OT</th>
<th>SI</th>
<th>SLP</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD</td>
<td>.254**</td>
<td>.182</td>
<td>.194**</td>
<td>.196**</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>.002</td>
<td>.061</td>
<td>.124</td>
<td>.129</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>.152*</td>
<td>.045</td>
<td>.054</td>
<td>.083</td>
</tr>
<tr>
<td>IVH</td>
<td>.245**</td>
<td>.239**</td>
<td>.230**</td>
<td>.101</td>
</tr>
<tr>
<td>NEC</td>
<td>.151*</td>
<td>.144*</td>
<td>.180**</td>
<td>.116</td>
</tr>
<tr>
<td>Other Brain Abnormality</td>
<td>.085</td>
<td>.089</td>
<td>.183**</td>
<td>.192**</td>
</tr>
<tr>
<td>ROP</td>
<td>.299**</td>
<td>.238**</td>
<td>.234**</td>
<td>.166**</td>
</tr>
<tr>
<td>Seizures</td>
<td>.088</td>
<td>.122*</td>
<td>.061</td>
<td>.038</td>
</tr>
<tr>
<td>Tone Abnormal</td>
<td>.087*</td>
<td>.132*</td>
<td>.105</td>
<td>.041</td>
</tr>
</tbody>
</table>

*Significant at the .05 level.  ** Significant at the .01 level.

Diagnoses Predicting Services, Above & Beyond Birthweight

Transition at Age 3 (N=135)

Demographics & Diagnosis: Followed Until 3 Years

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Yes, N=135</th>
<th>No, N=151</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>AA=93.2%</td>
<td>AA=87.7%</td>
</tr>
<tr>
<td>BW</td>
<td>Mean=1079.8g</td>
<td>Mean=1348g</td>
</tr>
<tr>
<td>GA</td>
<td>Mean &amp; Median=28wks</td>
<td>Mean &amp; Median=30wks</td>
</tr>
<tr>
<td>Sex</td>
<td>Males=48.1%</td>
<td>Males=54%</td>
</tr>
<tr>
<td>BPD</td>
<td>45.7%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Brain Lesion</td>
<td>5.5%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>5.4%</td>
<td>1.4%</td>
</tr>
<tr>
<td>IUGR</td>
<td>2.3%</td>
<td>2.9%</td>
</tr>
<tr>
<td>IVH</td>
<td>39%</td>
<td>21%</td>
</tr>
<tr>
<td>ROP</td>
<td>36.7%</td>
<td>19.6%</td>
</tr>
<tr>
<td>Tone Abnormal</td>
<td>3.1%</td>
<td>2%</td>
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</tbody>
</table>

Transition at Age 3 (N=135)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Part B</th>
<th>Don't Need Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male=63.8%</td>
<td>37%</td>
</tr>
<tr>
<td>Female</td>
<td>36.2%</td>
<td>63%</td>
</tr>
<tr>
<td>Race</td>
<td>African-American=92.9%</td>
<td>93.1%</td>
</tr>
<tr>
<td>BW</td>
<td>Median=993 grams</td>
<td>989 grams</td>
</tr>
<tr>
<td>Mean</td>
<td>1086.5 grams</td>
<td>1082.1 grams</td>
</tr>
<tr>
<td>Minimum</td>
<td>530 grams</td>
<td>535 grams</td>
</tr>
<tr>
<td>Maximum</td>
<td>2505 grams</td>
<td>2116 grams</td>
</tr>
<tr>
<td>GA</td>
<td>Median=27 weeks</td>
<td>27 weeks</td>
</tr>
<tr>
<td>Mean</td>
<td>283.2 weeks</td>
<td>28 weeks</td>
</tr>
<tr>
<td>Minimum</td>
<td>22 weeks</td>
<td>23 weeks</td>
</tr>
<tr>
<td>Maximum</td>
<td>36 weeks</td>
<td>35 weeks</td>
</tr>
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</table>
Diagnosis Correlated with Part B, Above & Beyond BW ≤1200g

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>PT</th>
<th>OT</th>
<th>SI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Lesion</td>
<td>.380*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIE</td>
<td>.380*</td>
<td>.422**</td>
<td></td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>.408*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>.380*</td>
<td>.422**</td>
<td></td>
</tr>
<tr>
<td>Tone Abnormal</td>
<td>.544**</td>
<td>.606**</td>
<td>.423**</td>
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Significance Level: *=.05, **=.01.

No significant correlations with diagnosis & SLP.

Service Distribution at Age 3 (N=135)

Comparison of Services

<table>
<thead>
<tr>
<th></th>
<th>All (N=135)</th>
<th>BW ≤1200g (N=94)</th>
<th>BW 1201-1500g (N=21)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Part C</td>
<td>Part B</td>
<td>Part C</td>
</tr>
<tr>
<td>Any</td>
<td>77%</td>
<td>45.9%</td>
<td>84%</td>
</tr>
<tr>
<td>PT</td>
<td>51.9%</td>
<td>15.6%</td>
<td>55.3%</td>
</tr>
<tr>
<td>OT</td>
<td>34.1%</td>
<td>14.1%</td>
<td>37.2%</td>
</tr>
<tr>
<td>SI</td>
<td>28.9%</td>
<td>20%</td>
<td>31.9%</td>
</tr>
<tr>
<td>SLP</td>
<td>48.9%</td>
<td>40%</td>
<td>54.3%</td>
</tr>
</tbody>
</table>

Conclusions

- Reinforces clinic policy of routinely following all infants born at <32 weeks gestation, under 1500g, and all infants with high-risk medical conditions (e.g., BPD, NEC) regardless of BW.
- Emphasizes need to routinely screen all developmental domains until at least 3 years.
- The inclusion of high probability conditions as an eligibility criteria is supported by the results of this study. Consideration should be given to adding BPD & NEC (surgical) to the existing list, & increasing birthweight to <1500g.
  - BPD & Surgical NEC are now accepted as High Probability conditions in Maryland.

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